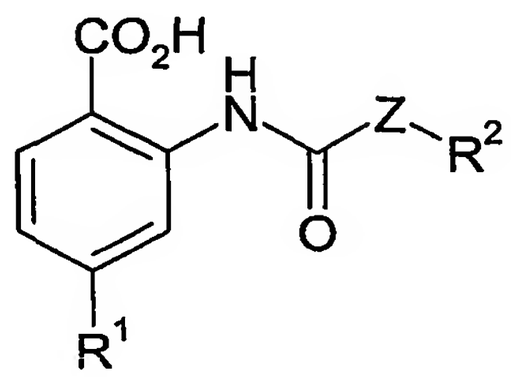
Claims

1. A compound selected from: a compound of Formula (I)



(I)

and a salt, solvate or physiologically functional derivative thereof, wherein:

R^1 represents hydrogen, halogen or C_1-C_3alkyl;

R^2 represents a 9 or 10-member saturated, partially saturated or unsaturated bi-cyclic ring system optionally including from 1 to 3 heteroatoms independently selected from S, O and N;

Z represents a linker unit selected from: $-(CH_2)_n-$; $-CH=CH-(CH_2)_m-$; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; $-(CH_2)_pO-$ and $-O-$;

n represents an integer selected from 2, 3 and 4;

m represents an integer selected from 0, 1 and 2;

p represents an integer selected from 1 and 2; and

R^3 represents hydrogen or C_1-C_4alkyl, with the proviso that when R^1 is H, Z is $-(CH_2)_n-$ and n = 2 or 3, R^2 is other than indol-3-yl.

2. A compound according to claim 1 wherein R^1 represents hydrogen, fluorine or methyl.

3. A compound according to claim 2 wherein R^1 represents hydrogen.

4. A compound according to any preceding claim wherein Z represents $-(CH_2)_pO-$ or $-(CH_2)_n-$.

5. A compound according to claim 4 wherein Z represents $-(CH_2)_n-$ and n represents an integer selected from 2, 3 or 4.

6. A compound according to claim 5 wherein Z is $-(CH_2)_n-$ and n is 2.

7. A compound according to claim 4 wherein Z represents $-(CH_2)_pO-$ and n represents 1.

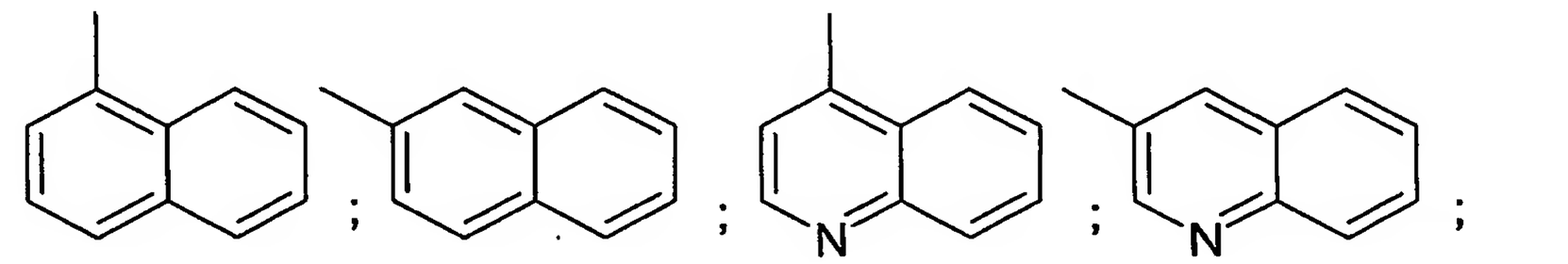
8. A compound according to any preceding claim wherein R^2 is a 10-member bi-cyclic ring system.

9. A compound according to claim 8 wherein R^2 is naphthyl.

10. A compound according claim 8 wherein R^2 is a 10-member ring system having either 1 or 2 heteroatoms.

11. A compound according to claim 10 wherein R^2 includes 1 or 2 nitrogen heteroatoms.

12. A compound according to any one of claims 9, 10 or 11 wherein R^2 is selected from the group consisting of: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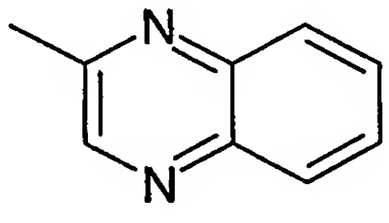
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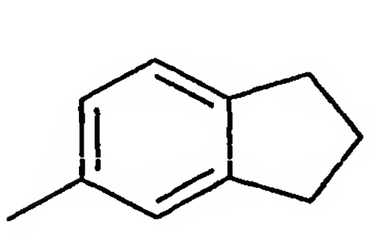
13. A compound according claim 8 wherein R^2 is substituted with one or more groups selected from C_1-C_2alkyl, -C(O)Me, =O and C_1-C_3alkoxy.

14. A compound according claim 13 wherein R^2 is substituted with one or more groups selected from methyl and methoxy.

15. A compound according any one of claims 1-7 wherein R^2 is a 9-member ring system selected from the group consisting of fused aryl-cycloalkyl, fused aryl and fused heteroaryl systems.

16. A compound according claim 15 wherein R^2 includes 1 to 3 heteroatoms selected from S, O or N.

17. A compound according to claim 15 or claim 16 wherein R^2 is selected from the group consisting of: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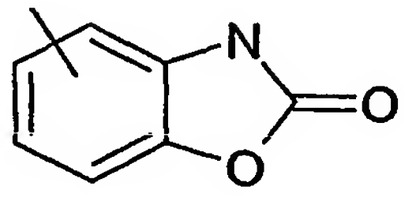
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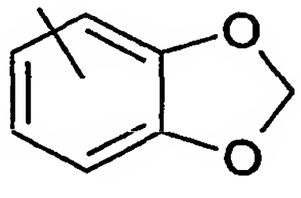
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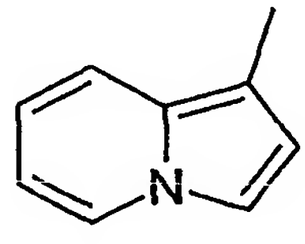
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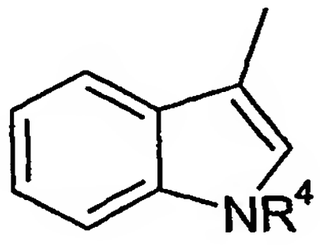
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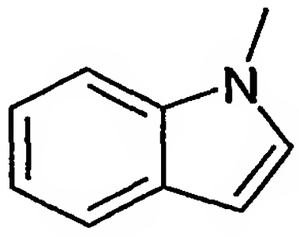
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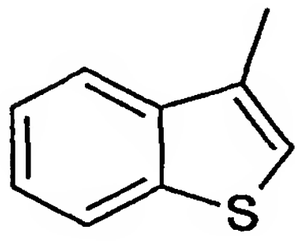
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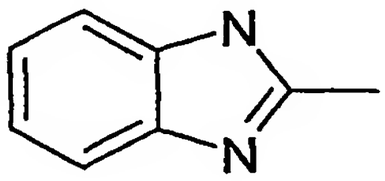
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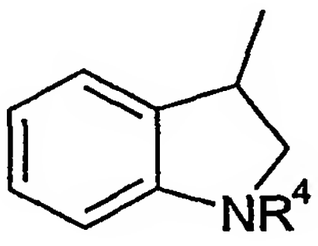
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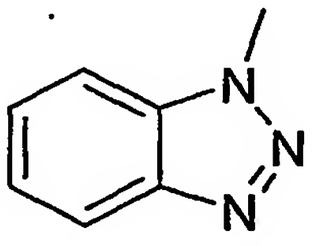
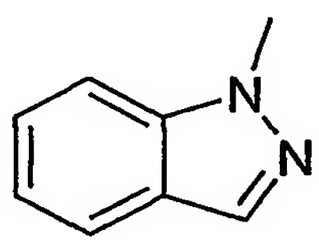
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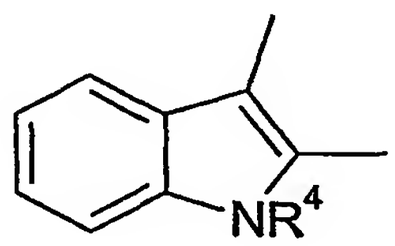


wherein R^4 represents hydrogen, methyl, CO_2H or CO_2Me.

18. A compound according to claim 17 wherein R^2 is substituted with one or more groups selected from C_1-C_3alkyl -C(O)Me, =O, C_1-C_3alkoxy, CO_2H and CO_2Me.

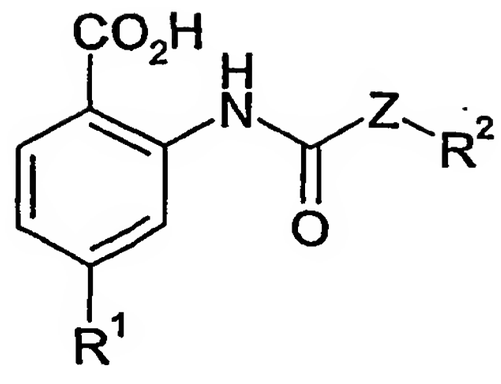
19. A compound according to claim 18 wherein R2 is substituted with methyl or methoxy.

20. A compound according to any preceding claim for use in human or veterinary medicine.

21. A compound according to any one of claims 1-19 for use in treating disorders of lipid metabolism including dislipidaemia and hyperlipoproteinaemia or in treating inflammatory diseases or conditions.

22. The use of a compound according to any one of claims 1-19 in the manufacture of a medicament for the treatment of disorders of lipid metabolism including dislipidaemia and hyperlipoproteinaemia or of inflammatory diseases or conditions.

23. A compound selected from: a compound of Formula (Ia)



(Ia)

and a salt, solvate or physiologically functional derivative thereof, wherein:

R^1 represents hydrogen, halogen or C_1-C_3alkyl;

R^2 represents a 9 or 10-member saturated, partially saturated or unsaturated bi-cyclic ring system optionally including from 1 to 3 heteroatoms independently selected from S, O and N;

Z represents a linker unit selected from: $-(CH_2)_n-$; $-CH=CH-(CH_2)_m-$; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; and $-O-$;

n represents an integer selected from 2, 3 and 4;

m represents an integer selected from 0, 1 and 2;

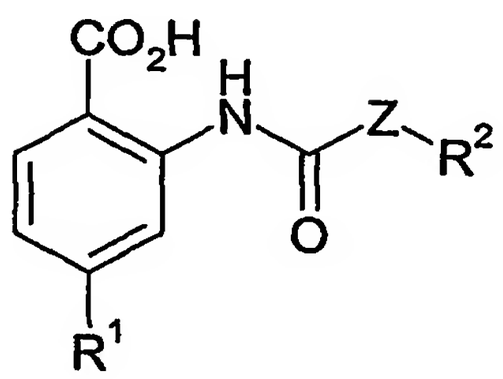
p represents an integer selected from 1 and 2; and

R^3 represents hydrogen or C_1-C_4alkyl,

for use in the treatment of disorders of lipid metabolism including dislipidaemia and hyperlipoproteinaemia or of inflammatory diseases or conditions.

24. A compound according to claim 23 for use in the treatment of diabetic dyslipidaemia, mixed dyslipidaemia, heart failure, hypercholesterolaemia, cardiovascular disease including atherosclerosis, arteriosclerosis, and hypertriglyceridaemia, coronary artery disease, thrombosis, angina, chronic renal failure, peripheral vascular disease and stroke, as well as the cardiovascular indications associated with type II diabetes mellitus, type I diabetes, insulin resistance, hyperlipidaemia, anorexia nervosa, obesity.

25. Use of a compound selected from: a compound of Formula (Ia)



(Ia)

and a salt, solvate or physiologically functional derivative thereof, wherein

R^1 represents hydrogen, halogen or C_1-C_3alkyl;

R^2 represents a 9 or 10-member saturated, partially saturated or unsaturated bi-cyclic ring system optionally including from 1 to 3 heteroatoms independently selected from S, O and N;

Z represents a linker unit selected from: $-(CH_2)_n-$; $-CH=CH-(CH_2)_m-$; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; and $-O-$;

n represents an integer selected from 2, 3 and 4;

m represents an integer selected from 0, 1 and 2;

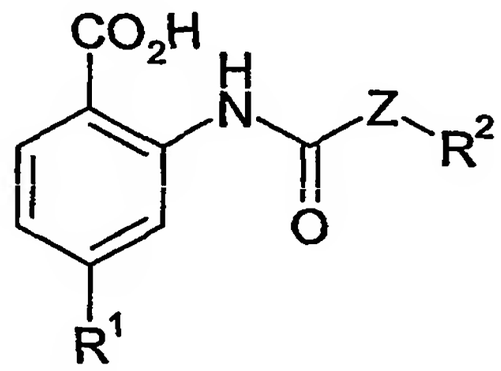
p represents an integer selected from 1 and 2; and

R^3 represents hydrogen or C_1-C_4alkyl,

in the manufacture of a medicament for the treatment of disorders of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or of inflammatory diseases or conditions.

26. The use of claim 25 wherein the disorder is selected from diabetic dyslipidaemia, mixed dyslipidaemia, heart failure, hypercholesterolaemia, cardiovascular disease including atherosclerosis, arteriosclerosis, and hypertriglyceridaemia, coronary artery disease, thrombosis, angina, chronic renal failure, peripheral vascular disease and stroke, as well as the cardiovascular indications associated with type II diabetes mellitus, type I diabetes, insulin resistance, hyperlipidaemia, anorexia nervosa and obesity.

27. A method for the treatment of a human or animal subject having a condition where under-activation of the HM74A receptor contributes to the condition or where activation of the receptor will be beneficial, which method comprises administering to said human or animal subject an effective amount of a compound selected from a compound of Formula (Ia)



(Ia)

and a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, wherein

R^1 represents hydrogen, halogen or C_1-C_3alkyl;

R^2 represents a 9 or 10-member saturated, partially saturated or unsaturated bi-cyclic ring system optionally including from 1 to 3 heteroatoms independently selected from S, O and N;

Z represents a linker unit selected from: $-(CH_2)_n-$; $-CH=CH-(CH_2)_m-$; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; and $-O-$;

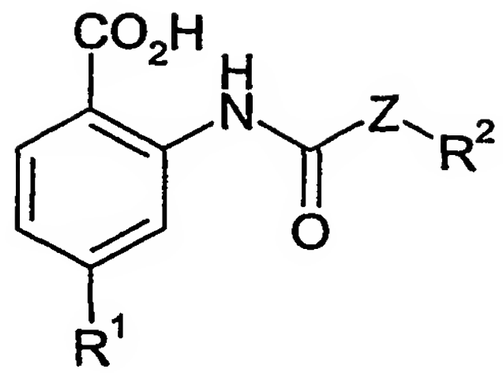
n represents an integer selected from 2, 3 and 4;

m represents an integer selected from 0, 1 and 2;

p represents an integer selected from 1 and 2; and

R^3 represents hydrogen or C_1-C_4alkyl.

28. A method for the treatment of a human or animal subject having a disorder of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or having an inflammatory disease or condition, which method comprises administering to said human or animal subject an effective amount of a compound selected from a compound of Formula (Ia)



(Ia)

and a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, wherein

R^1 represents hydrogen, halogen or C_1-C_3alkyl;

R^2 represents a 9 or 10-member saturated, partially saturated or unsaturated bi-cyclic ring system optionally including from 1 to 3 heteroatoms independently selected from S, O and N;

Z represents a linker unit selected from: $-(CH_2)_n-$; $-CH=CH-(CH_2)_m-$; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; and $-O-$;

n represents an integer selected from 2, 3 and 4;

m represents an integer selected from 0, 1 and 2;

p represents an integer selected from 1 and 2; and

R^3 represents hydrogen or C_1-C_4alkyl.

29. A pharmaceutical formulation comprising a compound according to any one of claims 1-19 in admixture with one or more physiologically acceptable diluents, excipients or carriers.

30. A combination for administration together or separately, sequentially or simultaneously in separate or combined pharmaceutical formulations, said combination comprising a compound according to any one of claims 1-19 together with another therapeutically active agent.

31. A pharmaceutical formulation comprising a compound according to any one of claims 1-19, a further active ingredient selected from the group consisting of statins, fibrates, bile-acid binding resins and nicotinic acid and one or more physiologically acceptable diluents, excipients or carriers.

32. A process for the preparation of a compound according to any one of claims 1-19, the method comprising the steps of:

i. alkylation of an aromatic alcohol with methyl 2-[(chloroacetyl)amino]benzoate
ii. hydrolysis of methyl ester using lithium hydroxide
iii. where desired or necessary converting a resultant free acid or base compound of formula (I) into a physiologically acceptable salt form or vice versa or converting one salt form into another physiologically acceptable salt form.

33. A process for the preparation of a compound according to any one of claims 1-19, the method comprising the steps of:

i. formation of an amide between the amine group of anthranilic acid (2-amino-bezoic acid) and an activated acyl transfer reagent derived from a carboxylic acid;

ii. where desired or necessary converting a resultant free acid or base compound of formula (I) into a physiologically acceptable salt form or vice versa or converting one salt form into another physiologically acceptable salt form.